

University of Groningen

Multiple flow profiles for two-phase flow in single microfluidic channels through site-selective channel coating

Logtenberg, Hella; Lopez-Martinez, Maria J.; Feringa, Ben L.; Browne, Wesley R.; Verpoorte, Elisabeth

Published in:

Lab on a Chip - Miniaturisation for Chemistry and Biology

DOI:

[10.1039/c1lc20012g](https://doi.org/10.1039/c1lc20012g)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version

Publisher's PDF, also known as Version of record

Publication date:

2011

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Logtenberg, H., Lopez-Martinez, M. J., Feringa, B. L., Browne, W. R., & Verpoorte, E. (2011). Multiple flow profiles for two-phase flow in single microfluidic channels through site-selective channel coating. *Lab on a Chip - Miniaturisation for Chemistry and Biology*, 11(12), 2030-2034. <https://doi.org/10.1039/c1lc20012g>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Cite this: *Lab Chip*, 2011, **11**, 2030

www.rsc.org/loc

TECHNICAL NOTE

Multiple flow profiles for two-phase flow in single microfluidic channels through site-selective channel coating†‡

Hella Logtenberg,^a Maria J. Lopez-Martinez,^b Ben L. Feringa,^a Wesley R. Browne^{*a} and Elisabeth Verpoorte^{*b}

Received 8th January 2011, Accepted 17th February 2011

DOI: 10.1039/c1lc20012g

An approach to control two-phase flow systems in a poly(dimethylsiloxane) (PDMS) microfluidic device using spatially selective surface modification is demonstrated. Side-by-side flows of ethanol : water solutions containing different polymers are used to selectively modify both sides of a channel by laminar flow patterning. Introduction of air pockets during modification allows for control over the length of the channel section that is modified. This approach makes it possible to achieve slug flow and side-by-side flow of water : 1-octanol simultaneously within the same PDMS channel, without the need of additional structural elements. A key finding is that conditioning of the PDMS channels with 1-octanol before polymer deposition is crucial to achieving stable side-by-side flows.

Introduction

The μL to nL volumes that enable precise control over temperature, reaction times and flow in microfluidic systems have driven their development over the last two decades towards the miniaturization of complex chemical and biochemical processes.¹ This is especially the case where sensitive, toxic or expensive reagents, or potentially hazardous reactions are involved, or where short preparation times and integrated work-up, e.g., extraction and concentration, are required, not least in the rapid multi-step synthesis of positron emission tomography (PET) radio-tracers.^{2,3} A key challenge in such systems is achieving efficient partitioning between immiscible solvent streams, thereby enabling rapid extraction and purification. This can be achieved using two-phase flow within microchannels and typically involves one of the two primary flow profiles, slug flow and side-by-side flow. Laminar flow, a characteristic feature of microfluidic channels, facilitates side-by-side solvent flows; however, it is slug flow, where the solvent of higher surface affinity encapsulates the second solvent to form droplets, that is the more commonly observed flow pattern in channels with uniform surface properties.

Continuous-flow chemical processing, as proposed by Kitamori and coworkers,⁴ achieves synthesis and extraction using

sequential contact and separation of side-by-side flowing immiscible solvents. With a sufficiently high degree of phase separation, separation of individual solvent streams could be maintained throughout a chip-based synthesis without the need for integration of an operation dedicated to separating slug flows. This generally requires stabilization through control of surface free energy, either by homogenous modification of glass channels, or by patterning surface free energies by formation of self-assembled monolayers, as described by Cheng and coworkers⁵ and Beebe and coworkers.^{6,7}

The interfacial contact areas between side-by-side flowing solvents are limited and require long channels for optimal partition of compounds between two solvents. Several design solutions to this problem have been reported to date, such as that of Jensen and co-workers.⁸ In their approach, mixing was achieved by a reduction in the diffusive path length by splitting and then recombining the solvent streams under slug flow conditions. Subsequent separation of the co-flowing streams employed capillary-pressure induced transport of one of the solvents across a thin, porous membrane that is impermeable to the other solvent. Kitamori and coworkers have used counter current flow and a guide structure to enhance the rate of partitioning and stabilize side-by-side flow.⁹

With slug flow, drag-induced rotation enhances rapid mass transport between phases;^{10–12} however, subsequent separation of solvents presents considerable design challenges.¹³ For effective partition and subsequent separation, the ideal design is a channel in which a switch can be made between slug and side-by-side flow. Recently, Takei *et al.*¹⁴ reported an elegant approach to this problem through patterned UV photocatalytic modification of coated titania particles immobilized on the walls of a microfluidic channel. In this system, surface wettability was controlled sufficiently to allow segmented flow followed by side-by-side flow, by

^aCenter for Systems Chemistry, Stratingh Institute for Chemistry, Faculty of Mathematics and Natural Sciences, University of Groningen, Nijenborgh 4, 9747 AG Groningen, The Netherlands. E-mail: w.r.browne@rug.nl

^bDepartment of Pharmacy, University of Groningen, Antonius Deusinglaan 1, 9713 AV Groningen, The Netherlands. E-mail: e.m.j.verpoorte@rug.nl

† Electronic supplementary information (ESI) available: Movie showing device in operation. See DOI: 10.1039/c1lc20012g

‡ Published as part of a LOC themed issue dedicated to Dutch Research: Guest Editor Professor Sabeth Verpoorte.

rendering one side of a channel superhydrophobic and the other side superhydrophilic. The challenge therefore is to achieve such behaviour by a direct surface modification method that circumvents conditions such as UV photopatterning to enable similar control to be achieved in non-UV transparent channels. In addition, from a fundamental perspective, it is important to ascertain how large a difference in surface free energy is actually necessary to achieve stable side-by-side flow.

In the present study, we focused on controlling water : 1-octanol two-phase flow due to its use in the determination of partition coefficients of drugs (logP values), an important indicator for the ability of drugs to cross the blood–brain barrier. The water : 1-octanol system has been traditionally used to mimic this barrier, due to 1-octanol being a hydrophobic compound whose structure resembles that of membrane lipids. Conventionally, partition coefficients are measured using liquid–liquid extraction, by agitating the two phases containing the compound in a separatory funnel or in shake flasks. After re-establishment of phase separation, the two phases are removed from the funnel or flask and the concentration of the compound of interest in each phase is determined. The ratio of these two concentrations defines the partition coefficient, logP. These partition coefficients are important factors for predicting the efficiency of, for example, anti-depressants.¹⁵ The conventional determination of partition coefficients by liquid–liquid extraction in a separatory funnel or shake flask is analyte-, solvent- and time-consuming. Microfluidic devices can decrease sample consumption into the nL range, and analysis time to a few minutes by providing increased contact areas for improved partitioning between phases.¹⁶ Effective mixing and good mass transfer rates are a prerequisite for such analysis¹² and hence, ideally, slug flow is employed. Several approaches have been reported using novel devices to separate the two phases using narrow, deep separation ducts, based on preferential filling of the ducts by one solvent by capillary forces when a pressure differential is applied.^{13,17,18} However, this requires a high-aspect-ratio device, and hence laser micromachining or other specialized techniques that are often not readily available. Alternatively, a porous hydrophobic membrane may be incorporated into the device, as described by Kralj *et al.*⁸ The organic phase passed through the membrane to exit through one outlet, leaving the aqueous phase behind to pass through a second outlet.

Here we demonstrate that *in situ* modification of straight microfluidic channels with polymers using a simple physisorption approach is sufficient to generate sequential slug and side-by-side flow patterns in a single microchannel (Fig. 1). In this approach, we make use of the stabilization of side-by-side flow in PDMS microchannels that we reported earlier,¹⁹ achieved by coating each half (along its length) of a channel with a different polymer. This straightforward approach takes advantage of the propensity

for unmodified channels to show slug flow and the induction of side-by-side flow by (partial) surface modification through localized physisorption of polymers.^{19,20} This simple approach circumvents the need for complex surface structuring of channels. The ability to switch flow profiles in a continuous flow system enables enhanced partition between merged immiscible solvent streams through slug flow, followed by subsequent phase separation into side-by-side flowing streams (Fig. 1).

Experimental section

Materials and instrumentation

All chemicals were purchased from Aldrich, Acros, or Fluka. All solvents used were analytical grade or better unless stated otherwise. A kit for making poly(dimethylsiloxane) (PDMS) (Sylgard 184 (Dow Corning)) devices was obtained from Mavom BV (Alphen aan de Rijn, The Netherlands). A PDMS : curing ratio of 10 : 1 was employed. Flow was generated using a New Era NE1600 syringe pump. The connection from the syringes containing the solvents and solutions to the microfluidic device was achieved using fused-silica capillaries (250 μm ID; 350 μm OD) and Upchurch Microtight adapters. Pictures were acquired using a Leica stereomicroscope with a DFC280 camera. FTIR spectroscopic studies were carried out using a Perkin Elmer Spectrum400 equipped with a PE/UATR (ZnSe/Diamond) attachment.

General procedure for device fabrication

The PDMS microfluidic devices were produced using a standard soft lithography process as described earlier, with the exception of the bonding process.¹⁹ Briefly, devices consisted of two PDMS layers, a flat unstructured bottom layer and a top layer containing the microchannel network and the fluidic feedthroughs for solvent interface connections. The channel network was made in PDMS by replication moulding. During this process, a PDMS prepolymer solution was cast onto a master consisting of a silicon wafer with a 100- μm -thick SU-8 photoresist layer patterned with the negative relief of the microchannel network. The PDMS (Sylgard 184 elastomer kit, Dow Corning, Midland, MI, USA) is supplied in two components, a silicon elastomer base and a curing agent. Both components were mixed in the standard ratio of 10 : 1 (base : curing agent, w/w) and the mixture was poured over the master and left to stand for 30 min to allow air bubbles to escape from the layer. Fluidic feedthroughs for capillary connections to the pump were prepared by positioning capillaries in the uncured PDMS on top of the SU-8 layer at the locations of the inlets and outlets of the device. The polyimide coating had been removed by burning from the ends of these capillaries. A Perspex plate with a hole pattern drilled corresponding to the placement of the capillaries was placed over the replication master, and used to position and hold the capillaries in place during the curing of the PDMS. The PDMS microchannel layer was fully cured at 35 $^{\circ}\text{C}$ overnight. The capillaries were then removed by applying a drop of toluene to the PDMS at the location of the capillaries. After 1 min, the capillaries were carefully pulled from the PDMS.

The bottom layer was made by curing the PDMS on a smooth bare silicon wafer overnight at room temperature. This resulted

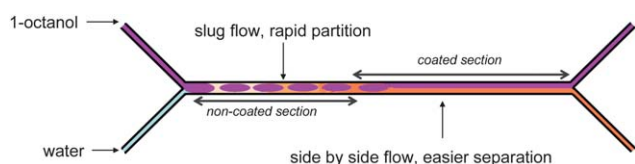


Fig. 1 Combining slug flow and side-by-side flow in one channel.

in a sticky layer which was only partially cured. Bonding was accomplished by placing the microchannel layer, channels down, on top of the sticky layer, and heating the assembly for another 30 min at 60 °C to allow for the formation of covalent bonds between the sticky and cured PDMS layers. The resulting sealed channels were 200 μm wide, 100 μm high, and 4 cm long. It should be noted that bonding using UV-ozone treatment was found to result in a more hydrophilic and brittle PDMS surface in the channel that was unsuitable for the surface modification procedures employed in the present study.

General procedure for coating of microfluidic channels with two different polymers

Two polymer solutions were prepared using the high-molecular-weight polymers poly(vinyl pyrrolidone) (PVP) and poly(2-hydroxyethylmethacrylate) (pHEMA), both 10 mg mL⁻¹ in a 1 : 1 H₂O : ethanol solution. The channels were either used directly or conditioned by first flowing 1-octanol through the channels and leaving filled for at least 15 min, after which the 1-octanol was removed by flushing with water/ethanol (1/1, v/v, Fig. 2). Filling for shorter periods was found to result in less reliable flow profiles. The polymer solutions were introduced into the channel from different inlets and flowed side-by-side at a constant flow rate of 2 $\mu\text{L min}^{-1}$. After flushing the channels for 5 min, the flow was stopped, and the devices were left to stand for 2 hours to ensure adequate physisorption of the polymers onto channel surfaces. When only partial coating of a channel segment was required, an air bubble was introduced immediately after flow was stopped by using a syringe filled with air. This was done by first removing both the capillaries used for introducing the solvent. Both inlets were then emptied by applying air pressure using an empty syringe at one inlet of the channel. Afterwards, one inlet was blocked and the other inlet was used to introduce the air pocket into the channel. The channels were left for two

hours in a sealed container, together with a moist tissue, to inhibit evaporation. The polymer solutions were then removed by applying air pressure using an empty syringe at the inlet of the channel and the channels were ready for the study of water : 1-octanol flow behaviour.

Contact-angle studies

Contact angle experiments were performed using a Dataphysics OCA30. The coating procedure as used for the partition device was applied to microchannels suitable for contact-angle experiments. These channels had dimensions of 1 mm in width and 100 μm in height. The channels were prepared and bonded as reported in the section on device fabrication and then coated with either of the two polymers as described above. The device was then sliced between the two layers of PDMS to expose the channel surfaces. Both channel and cover pieces were tested. A drop of water or 1-octanol (0.2 μL) was deposited on the modified regions of both PDMS pieces (Fig. 3). In addition, flat, unstructured pieces of PDMS were coated directly with polymer solution for comparison. Contact angles were determined immediately following polymer coating and after several hours. The contact angles determined immediately and after ageing were identical.

Water : 1-octanol fuchsine dye partition studies

The fuchsine dye was dissolved in 1-octanol (5 mg mL⁻¹). 1-Octanol was introduced at the PVP-coated side of the channel and water was introduced at the pHEMA-coated side of the channel. Upon partition the water phase turned orange (Fig. 4), which provided for good contrast with respect to the pink-coloured 1-octanol phase. Total flow rates between 0.5 and 2 $\mu\text{L min}^{-1}$ as well as differential solvent flow rate ratios between 1 : 1 and 3 : 1 water : 1-octanol were tested. Although the rate of partition varied, the flow profile was independent of the flow rate.

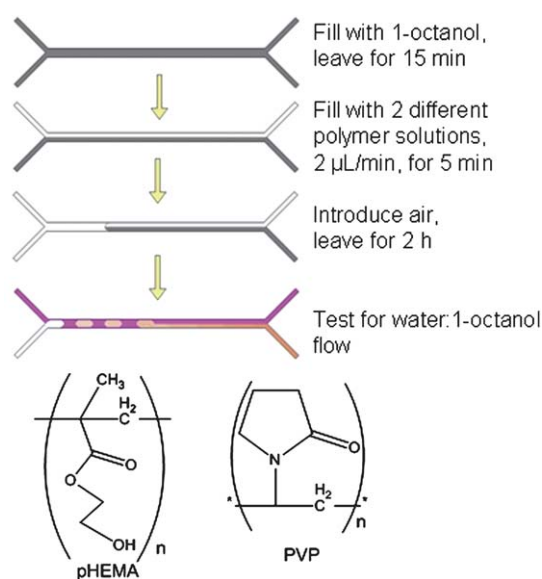


Fig. 2 Surface modification employs four sequential treatment steps to locally coat two water-soluble polymers pHEMA and PVP onto a microfluidic channel.

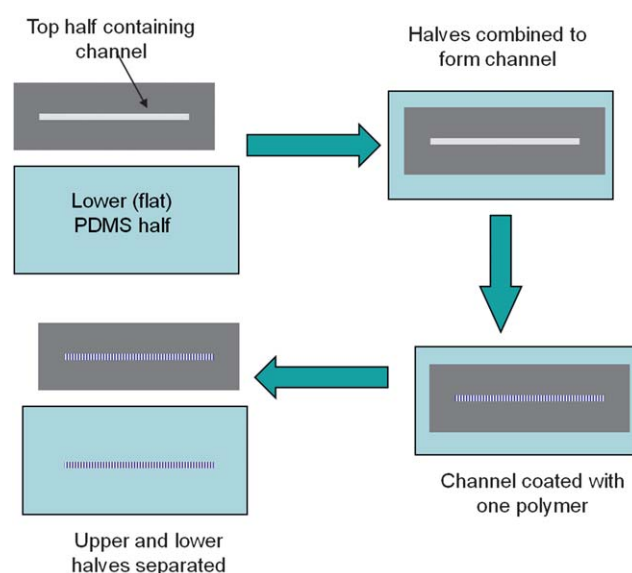


Fig. 3 Procedure for preparing polymer-coated channels for surface solvent contact angle determination.

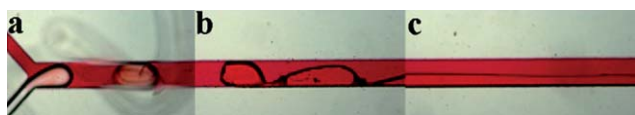


Fig. 4 Spatially controlled physisorption of two polymers in a microchannel allows for switching between slug flow and side-by-side flow. Partition of fuchsin dye between water (entering from bottom inlet) and 1-octanol streams (entering with dye from the top inlet): (a) start of the channel, slug flow, followed (b) by a slug to side-by-side flow transition, and then (c) side-by-side flow is maintained. Channels are 200 μm wide and 100 μm high. See also ESI†.

Results and discussion

Previously we reported the stabilization of 1-octanol : water side-by-side streams in microchannels in poly(dimethylsiloxane) (PDMS) chips through physisorption of high-molecular-weight polymers to the channel's surface.¹⁹ For 1-octanol : water systems, native PDMS²¹ exhibits slug-flow behaviour,¹⁹ which improves extraction, but renders separation of slugs into separate channel streams challenging. In our approach, heterogeneous coating with two different polymer solutions, PVP (30 kDa) and pHEMA (1 MDa), provides for a stable side-by-side flow and effective separation of the two solvent streams.

In this report we employ this technique to effect sequential slug flow and side-by-side flow along a single channel by controlling spatially the physisorption of polymers on the channel surfaces (Fig. 2). Surface modification employs a laminar-flow patterning approach. PDMS microfluidic channels were filled with two different polymer solutions (*i.e.* PVP and pHEMA, both as aqueous ethanol solutions), with each solution entering *via* a separate inlet to merge in the channel to be modified (Fig. 2). Due to the laminar flow behaviour inside the microfluidic channel, the interface between the two solutions runs along the centre line of the channel when equal flow rates are employed. A pocket of air is then introduced into a defined length of the channel followed by standing for 2 h, to allow for polymer physisorption. Diffusion of either polymer into its neighbouring stream during the physisorption process is negligible, due to the extremely small diffusion coefficients of these large molecules. Polymer deposition is thus localized, with one polymer coating one side of the channel, the other polymer coating the other side. Importantly, by introducing air pockets into the channel immediately after filling with the polymer solutions, the spatial distribution of polymer physisorption along the channel's length is also controlled (Fig. 2).

The water : 1-octanol flow behaviour in the modified channels was assessed through monitoring the partitioning of fuchsin dye introduced in the 1-octanol phase (colouring this phase, Fig. 4a). The section of the channel where an air pocket was introduced during modification exhibited slug flow behaviour typical of an uncoated PDMS channel and showed the partition of the fuchsin dye into the water layer. In the section where polymer modification (Fig. 4c) had been performed, side-by-side flow was observed with a short transition region between flow patterns (Fig. 4b); see also ESI† for a movie showing this.

Several channels were tested with respect to coating stability. The channels, pre-treated with 1-octanol prior to coating, showed similar flow profiles for periods of continuous flow for longer than 2 h. Several chips were subsequently emptied and stored under

ambient conditions for periods of one week to four months. All channels showed stable flow profiles after storage. Despite the fact that ethanol/water mixtures were used to coat the channels with the polymers, rinsing the coated channels with water or ethanol did not influence the observed water : 1-octanol flow profile. This is expected, since the rate of desorption of the polymer is expected to be low due to the multiple interactions between the physisorbed polymer and the PDMS. That this is the case is supported by the observation that rinsing with isopropanol results in destabilization of the side-by-side flow, indicating that the coating of physisorbed polymers is partly removed from the surfaces by this treatment.

Separation of the water and the 1-octanol phase at the end of the modified channel was incomplete with both the T- or the Y-shaped outlets due to the low interfacial pressure between water and 1-octanol, as reported previously by Cheng *et al.* when using water : ethyl acetate mixtures.⁵ However, since this aspect is outside the scope of this study, optimization of phase separation was not pursued further in our devices. Using the model proposed by Kitamori *et al.* for calculation of phase separation based on the interfacial pressure balance, it is expected that for solvent combinations with higher interfacial pressure differences the separation will be more efficient.²² Overall, however, flow profiles were not influenced by inlet and outlet geometries, with no differences observed between Y and T configurations.

The ability for physisorbed polymer coatings to switch flow from slug to side-by-side flow suggests variation in surface energy. Hence, a difference in contact angle would be anticipated, given the effect on the flow profile these modified surfaces impose within microfluidic devices. Solvent contact angles were determined to investigate the effect of surface modification on surface solvent interaction. PDMS channels suitable for contact angle studies (see Experimental section) were coated homogeneously using only one of the polymer solutions in each case and cut open horizontally. Typical contact angles measured for water on untreated PDMS were $110 \pm 10^\circ$. It is important to note that although the uncertainty in contact angle is $\pm 2^\circ$ for an individual sample, the variation observed between different samples of PDMS is larger. Though conditioning of the channel with 1-octanol lowered the contact angle for water to 96° , measured contact angles for water on polymer-coated PDMS showed values within experimental uncertainty, both $110 \pm 10^\circ$ for water on PVP-coated and pHEMA-coated PDMS. Contact angles determined for 1-octanol on untreated PDMS and on PVP- or pHEMA-coated PDMS were $35 \pm 5^\circ$. Overall, since the differences observed between different polymer coated surfaces are within the experimental error for contact angle measurements, it is apparent that the differences in surface properties required to change flow profiles within microfluidic devices are equally small. It is possible that the mechanism for deposition in the microchannel may be different than on a bulk flat surface. For this reason, flat pieces of PDMS (*i.e.* not in a channel) were also modified with the polymer; however, the contact angles measured for these samples were equivalent to those determined for the channels. This indicates that coating of the channel walls is essentially the same as coating of a bulk surface. These results are remarkable, as it would be expected that a change in surface hydrophobicity/philicity would be essential to achieve the side-by-side flow patterns observed; this is not in fact the case.

The work of Takei *et al.*¹⁴ would seem to indicate that a large difference in hydrophobicity/hydrophilicity between the two

surfaces is required to achieve stable side-by-side flow. In the present system, however, we achieve similar flow behaviour but with no measurable difference in the contact angles for the two polymer coatings deposited on the PDMS channel walls. Hence, the simple assumption that fluid flow is dependent on wettability is not necessarily valid. These results could be rationalized, however, by considering that partial masking of surface charge by the polymers could sufficiently, albeit not completely, dictate solvent flow. It should be noted also that wettability, as determined by the solvent contact angle, is ultimately dependent on the overall surface composition especially at the edge of the solvent drop.

An important observation is the role of 1-octanol conditioning. The complex flow behaviour observed subsequent to channel modification required that the channels were flushed with 1-octanol prior to the coating procedure (Fig. 2). In channels that were not conditioned with 1-octanol prior to introducing the polymer solutions, the side-by-side flow achieved with water : 1-octanol was not stable enough to achieve full two-phase, side-by-side flow. The results are shown in the images in Fig. 5.

The specific role of the 1-octanol conditioning may be to improve adhesion of the polymers; however, it is presently not understood. From FTIR ATR spectroscopy, it can be determined that the 1-octanol and indeed the polymers are present at most in sub-monolayer levels (*i.e.* below detection limits). Furthermore there is no evidence for swelling with 1-octanol. However, 1-octanol conditioning of PDMS results in a change in contact angle. A possible explanation for the effect of 1-octanol conditioning is that it renders the channels more hydrophilic (*i.e.* lower water contact angle) facilitating adsorption of the polymers to the channel walls. Notably, although conditioning with 1-octanol decreases the contact angle for water, this pretreatment is in itself insufficient to obtain stable side-by-side flow patterns.

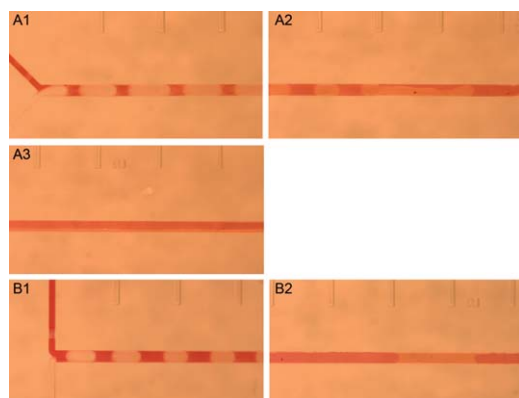


Fig. 5 Two channels, which were prepared from the same batch of PDMS, were compared to assess the influence of conditioning with 1-octanol prior to polymer coating. Channel A was filled and left with 1-octanol for 15 min. Channel B was flushed with water : ethanol prior to the coating. Subsequently, both channels were coated as described above (heterogeneous, PVP and pHEMA, filled at $2 \mu\text{L min}^{-1}$, flow stopped followed by introduction of an air pocket to half-way along the channel, left for 2 h). (A1) Start of the channel, slug flow, followed by (A2) a slug to side-by-side flow transition, and then (A3) side-by-side flow is maintained. (B1) Start of channel, slug flow, followed by (B2) elongated slugs, but side-by-side flow is not obtained.

Conclusions

We demonstrate a simple yet effective method to control the flow behaviour of two immiscible solvents inside a PDMS-based microfluidic channel, and importantly, switch between flow profiles. This is achieved *via* local physisorption of high-molecular-weight polymers to the PDMS walls of the channel using a laminar-flow patterning approach, circumventing the need for destructive UV irradiation or other forms of lithography. These polymer coatings stabilize side-by-side two-phase flow. The flow behaviour can be tailored to specific requirements simply by controlling the location of modification. Future studies will be directed at extending this approach to other channel materials such as glass. Understanding the role of 1-octanol conditioning of the channel and the surface coverage of the polymers in our PDMS devices may prove necessary to achieve this key next step.

The present approach to combine slug and side-by-side flow patterns in a single channel is technically simple and readily accessible, and importantly, it makes use of tuning of the surface energy after construction of a device. These features allow for the rapid optimization of coating conditions and hence faster prototyping possibilities.

Acknowledgements

We thank L.C. Jellema for discussion, NWO Vidi (H.L. and W.R.B.) and NanoNed (B.L.F.) for financial support.

Notes and references

- 1 G. M. Whitesides, *Nature*, 2006, **442**, 368.
- 2 C.-C. Lee, G. Sui, A. Elizarov, C. J. Shu, Y.-S. Shin, A. N. Dooley, J. Huang, A. Daridon, P. Wyatt, D. Stout, H. C. Kolb, O. N. Witte, N. Satyamurthy, J. R. Heath, M. E. Phelps, S. R. Quake and H.-R. Tseng, *Science*, 2005, **310**, 1793.
- 3 R. L. Hartman and K. F. Jensen, *Lab Chip*, 2009, **9**, 2495.
- 4 M. Tokeshi, T. Minagawa, K. Uchiyama, A. Hibara, K. Sato, H. Hisamoto and T. Kitamori, *Anal. Chem.*, 2002, **74**, 1565.
- 5 H. Xiao, D. Liang, G. Liu, M. Guo, W. Xing and J. Cheng, *Lab Chip*, 2006, **6**, 1067.
- 6 B. Zhao, J. S. Moore and D. J. Beebe, *Science*, 2001, **291**, 1023.
- 7 B. Zhao, N. O. L. Viernes, J. S. Moore and D. J. Beebe, *J. Am. Chem. Soc.*, 2002, **124**, 5284.
- 8 J. G. Kralj, H. R. Sahoo and K. F. Jensen, *Lab Chip*, 2007, **7**, 256.
- 9 A. Aota, M. Nonaka, A. Hibara and T. Kitamori, *Angew. Chem., Int. Ed.*, 2007, **46**, 878.
- 10 J. R. Burns and C. Ramshaw, *Lab Chip*, 2001, **1**, 10.
- 11 H. Song, J. D. Tice and R. F. Ismagilov, *Angew. Chem., Int. Ed.*, 2003, **42**, 768.
- 12 M. Surmeian, A. Hibara, M. Slyadnev, K. Uchiyama, H. Hisamoto and T. Kitamori, *Anal. Lett.*, 2001, **34**, 1421.
- 13 A. Günther, M. Jhunjhunwala, M. Thalmann, M. A. Schmidt and K. F. Jensen, *Langmuir*, 2005, **21**, 1547.
- 14 G. Takei, A. Aota, A. Hibara, T. Kitamori and H.-B. Kim, Conference Proceedings, microTas2007, 2007, 1213.
- 15 C. Hansch and T. Fujita, *J. Am. Chem. Soc.*, 1964, **86**, 1616.
- 16 K. Carlsson and B. Karlberg, *Anal. Chim. Acta*, 2000, **423**, 137.
- 17 D. M. Fries, T. Voigt and P. R. von Rohr, *Chem. Eng. Technol.*, 2008, **31**, 1182.
- 18 O. K. Castell, C. J. Allender and D. A. Barrow, *Lab Chip*, 2009, **9**, 388.
- 19 H. J. van der Linden, L. C. Jellema, M. Holwerda and E. Verpoorte, *Anal. Bioanal. Chem.*, 2006, **385**, 1376.
- 20 I. Wong and C.-M. Ho, *Microfluid. Nanofluid.*, 2009, **7**, 291.
- 21 J. C. McDonald and G. M. Whitesides, *Acc. Chem. Res.*, 2002, **35**, 491.
- 22 A. Aota, K. Mawatari, S. Takahashi, T. Matsumoto, K. Kanda, R. Anraku, A. Hibara, M. Tokeshi and T. Kitamori, *Microchim. Acta*, 2009, **164**, 249.